

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>KP/3283 PCT</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/GB 99/00967</b>	International filing date (day/month/year) <b>26/03/1999</b>	(Earliest) Priority Date (day/month/year) <b>27/03/1998</b>
Applicant <b>ISIS INNOVATION LIMITED et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☒ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

**POLYMORPHISM III: LINKAGE OF ATOPY TO A LOCUS ON CHROMOSOME 13**

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB 99/00967

**Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Claim 10 refers to chromosome 2. This appears to be an inadvertent error: it was assumed that this should have been chromosome 13.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International Application No

T/GB 99/00967

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 6 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
 IPC 6 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MARONE G: "Asthma: recent advances" TRENDS IMMUNOLOGY TODAY, vol. 19, no. 1, January 1998 (1998-01), pages 1-5, XP004101456 page 1, paragraph 2 ---	1
A	WILTSHIRE S ET AL: "A genome scan for loci influencing total serum immunoglobulin levels: possible linkage of IgA to the chromosome 13 atopy locus" HUMAN MOLECULAR GENETICS, vol. 7, no. 1, January 1998 (1998-01), pages 27-31, XP002110729 see "Discussion" --- -/--	1



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## ° Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance  
 "E" earlier document but published on or after the international filing date  
 "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  
 "O" document referring to an oral disclosure, use, exhibition or other means  
 "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

29 July 1999

Date of mailing of the international search report

10/08/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Osborne, H

## INTERNATIONAL SEARCH REPORT

International Application No

T/GB 99/00967

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DANIELS S ET AL: "A genome-wide search for quantitative trait loci underlying asthma " NATURE, vol. 383, 1996, pages 247-50, XP002110730 cited in the application the whole document ---	1-14
A	ABRAMSON M ET AL: "The new asthma genetics and its implications for public health" PUBLIC HEALTH REVIEW, vol. 26, no. 2, February 1998 (1998-02), pages 127-144, XP002110731 see abstract and page 137, para 4 to page 138 ---	1-14
A	WO 95 05481 A (ISIS INNOVATION LTD.) 23 February 1995 (1995-02-23) cited in the application the whole document ---	1-14
A	DIB C ET AL: "A comprehensive genetic map of the human genome based on 5264 microsatellites" NATURE, vol. 380, 14 March 1996 (1996-03-14), pages 152-154, XP002110732 -----	

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/00967

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9505481 A	23-02-1995	NONE	

## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

WILKINSON, John, Stephen  
Stevens, Hewlett & Perkins  
1 Augustine's Place  
Bristol BS1 4UD  
ROYAUME-UNI

Date of mailing (day/month/year)

03 February 2000 (03.02.00)

Applicant's or agent's file reference

KP/3283 PCT

International application No.

PCT/GB99/00967

## IMPORTANT NOTIFICATION

International filing date (day/month/year)

26 March 1999 (26.03.99)

1. The following indications appeared on record concerning:

☐

the applicant

☐

the inventor

☒

the agent

☐

the common representative

Name and Address

PRIVETT, Kathryn, Louise  
Stevens, Hewlett & Perkins  
1 Serjeants' Inn  
Fleet Street  
London EC4Y 1NT  
United Kingdom

State of Nationality

State of Residence

Telephone No.

0171 936 2499

Facsimile No.

0171 936 2498

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐

the person

☒

the name

☒

the address

☐

the nationality

☐

the residence

Name and Address

WILKINSON, John, Stephen  
Stevens, Hewlett & Perkins  
1 Augustine's Place  
Bristol BS1 4UD  
United Kingdom

State of Nationality

State of Residence

Telephone No.

117 922 6007

Facsimile No.

117 922 6009

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒

the receiving Office

☐

the International Searching Authority

☒

the International Preliminary Examining Authority

☐

the designated Offices concerned

☒

the elected Offices concerned

☐

other:

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

I. Britel

Telephone No.: (41-22) 338.83.38

09/647330

**PCT**

From the INTERNATIONAL BUREAU

**NOTIFICATION OF THE RECORDING  
 OF A CHANGE**

(PCT Rule 92bis.1 and  
 Administrative Instructions, Section 422)

To:

CORNISH, Kristina  
 Kilburn & Strode  
 20 Red Lion Street  
 London WC1R 4PJ  
 ROYAUME-UNI

<b>Date of mailing</b> (day/month/year) 29 September 2000 (29.09.00)	<b>IMPORTANT NOTIFICATION</b>
<b>Applicant's or agent's file reference</b> KP/3283 PCT	
<b>International application No.</b> PCT/GB99/00967	<b>International filing date</b> (day/month/year) 26 March 1999 (26.03.99)

1. The following indications appeared on record concerning:

☐ the applicant ☐ the inventor ☒ the agent ☐ the common representative

Name and Address

WILKINSON, John, Stephen  
 Stevens, Hewlett & Perkins  
 Halton House  
 20/23 Holborn  
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 United Kingdom

State of Nationality

State of Residence

Telephone No.

+44 20 7404 1955

Facsimile No.

+44 20 7404 1844

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☒ the person ☐ the name ☐ the address ☐ the nationality ☐ the residence

Name and Address

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 20 Red Lion Street  
 London WC1R 4PJ  
 United Kingdom

State of Nationality

State of Residence

Telephone No.

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Facsimile No.

+44 20 7539 4299

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned  
☐ the International Searching Authority ☒ the elected Offices concerned  
☐ the International Preliminary Examining Authority ☐ other:

<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	<b>Authorized officer</b>  Jean-Marie McAdams  Telephone No.: (41-22) 338.83.38
--	---

09/647330

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

CORNISH, Kristina  
Kilburn & Strode  
20 Red Lion Street  
London WC1R 4PJ  
ROYAUME-UNI

Date of mailing (day/month/year)

31 October 2000 (31.10.00)

Applicant's or agent's file reference

KP/3283 PCT

International application No.

PCT/GB99/00967

## IMPORTANT NOTIFICATION

International filing date (day/month/year)

26 March 1999 (26.03.99)

1. The following indications appeared on record concerning:

☒

the applicant

☐

the inventor

☐

the agent

☐

the common representative

Name and Address

ISIS INNOVATION LIMITED  
2 South Parks Road  
Oxford OX1 3UB  
United Kingdom

State of Nationality

GB

State of Residence

GB

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐

the person

☐

the name

☒

the address

☐

the nationality

☐

the residence

Name and Address

ISIS INNOVATION LIMITED  
Ewert House  
Ewert Place  
Summertown  
Oxford OX2 7BZ  
United Kingdom

State of Nationality

State of Residence

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒

the receiving Office

☐

the International Searching Authority

☐

the International Preliminary Examining Authority

☐

the designated Offices concerned

☒

the elected Offices concerned

☐

other:

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Peggy Steunenberg

Telephone No.: (41-22) 338.83.38



## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C. 20231  
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 02 December 1999 (02.12.99)	
<b>International application No.</b> PCT/GB99/00967	<b>Applicant's or agent's file reference</b> KP/3283 PCT
<b>International filing date</b> (day/month/year) 26 March 1999 (26.03.99)	<b>Priority date</b> (day/month/year) 27 March 1998 (27.03.98)
<b>Applicant</b> COOKSON, William, Osmond, Charles, Michael et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
27 October 1999 (27.10.99)

☐ in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer J.M. Vivet</p> <p>Telephone No.: (41-22) 338.83.38</p>
--	--

## PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

To:

WILKINSON, John, Stephen  
Stevens, Hewlett & Perkins  
Halton House  
20/23 Holborn  
London, EC1N 2JD  
ROYAUME-UNI

Date of mailing (day/month/year)  
19 April 2000 (19.04.00)

Applicant's or agent's file reference  
KP/3283 PCT

## IMPORTANT NOTIFICATION

International application No.  
PCT/GB99/00967

International filing date (day/month/year)  
26 March 1999 (26.03.99)

## 1. The following indications appeared on record concerning:

☐ the applicant ☐ the inventor ☒ the agent ☐ the common representative

Name and Address

WILKINSON, John, Stephen  
Stevens, Hewlett & Perkins  
1 Augustine's Place  
Bristol BS1 4UD  
United Kingdom

State of Nationality

State of Residence

Telephone No.

117 922 6007

Facsimile No.

117 922 6009

Teleprinter No.

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☒ the address ☐ the nationality ☐ the residence

Name and Address

WILKINSON, John, Stephen  
Stevens, Hewlett & Perkins  
Halton House  
20/23 Holborn  
London, EC1N 2JD  
United Kingdom

State of Nationality

State of Residence

Telephone No.

+44 20 7404 1955

Facsimile No.

+44 20 7404 1844

Teleprinter No.

## 3. Further observations, if necessary:

## 4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned  
☐ the International Searching Authority ☒ the elected Offices concerned  
☒ the International Preliminary Examining Authority ☐ other:

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

I. Britel

Telephone No.: (41-22) 338.83.38

5  
REC'D 27 JUN 2000



WIPO

PCT

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PP/NT/PH/3283		<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB99/00967	International filing date (day/month/year) 26/03/1999	Priority date (day/month/year) 27/03/1998	
International Patent Classification (IPC) or national classification and IPC C12Q1/68			
Applicant ISIS INNOVATION LIMITED et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 4 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 2 sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"><li>I <input checked="" type="checkbox"/> Basis of the report</li><li>II <input type="checkbox"/> Priority</li><li>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li><li>IV <input type="checkbox"/> Lack of unity of invention</li><li>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li><li>VI <input type="checkbox"/> Certain documents cited</li><li>VII <input type="checkbox"/> Certain defects in the international application</li><li>VIII <input checked="" type="checkbox"/> Certain observations on the international application</li></ul>			
Date of submission of the demand  27/10/1999		Date of completion of this report  23.06.2000	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer  Hinchliffe, P  Telephone No. +49 89 2399 8431 	

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB99/00967

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-10 as originally filed

**Claims, No.:**

1-14 as received on 08/05/2000 with letter of 08/05/2000

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes:	Claims	1-14
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-14
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	10-14
	No:	Claims	1-9

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB99/00967

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**2. Citations and explanations**

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

## **SECTION V**

1. The closest prior art document appears to be WO 95 05481 (D5 as cited in the ISR). The document discloses a method identical to the one claimed but using a different marker. Although the region where the new marker was located (chromosome 13) was intensively studied, the exact marker currently used had not been disclosed. Consequently the subject matter of the claims appears to fulfill the requirements of Articles 33(2) and 33(3) PCT.
2. Claims 1-9 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

## **SECTION VIII**

1. The term "suitably stringent", found in claim 12, is unclear contrary to Art 6. PCT and thus it should be clarified by reference to the exact hybridisation conditions necessary.
2. The term "substantially similar sequences", found in claim 13, is unclear contrary to Art 6. PCT.
3. In order for the subject matter of claim 10 to be assured of novelty it should be shown that the term "up to 1Mb....which region contains D13S273" does not happen to include the probe D13S153 disclosed in D2 (as cited in the ISR).
4. The disclaimer found in claim 10 should also appear in claim 1.
5. The reference to the probe (i.e. where it can be found) should also be included in the claims for reasons of clarity.
6. The reference to D13S273\*4 is considered to be unclear and consequently the reference to the sequence given in the text should be included into the claim (see page 8) in order to overcome a problem of clarity.

**CLAIMS**

1. A method for diagnosing an individual as being atopic, or as having a predisposition to atopy, which method comprises demonstrating in a nucleic acid sample taken from an individual the presence or absence of an allele which is associated with atopy, wherein the allele is situated at a locus in a region of chromosome 13 of up to 1 megabase in length, which region contains the locus D13S273, the presence of the allele D13S273\*4 being indicative of a predisposition to asthma.
2. The method according to claim 1, wherein the method comprises the steps of:
  - (i) obtaining a suitable tissue sample from the individual;
  - (ii) preparing from the tissue sample a nucleic acid sample;
  - (iii) analysing the nucleic acid sample for the presence or absence of the allele.
3. The method according to claim 2, wherein prior to analysis, the locus at which the allele is situated is amplified.
4. The method according to claim 3, wherein the amplification is by the PCR.
5. The method according to any one of the claims 1 to 4, wherein the locus at which the allele is situated comprises microsatellite repeats of variable lengths.
6. The method according to claim 4 or claim 5, wherein amplification is performed using a pair of primers each of which hybridise under suitably stringent conditions to a region either side of the microsatellite repeats.

7. The method according to any one of claims 1 to 6, wherein the allele for identification is D13S273\*4.
8. The method according to any one of claims 3 to 7, wherein the analysis is carried out by size separation of amplification products.
9. The method according to claim 7, wherein the primers in the pair of primers comprise the oligonucleotide sequences identified by SEQ ID NO: 1 and SEQ ID NO: 2 or substantially similar sequences.
10. A pair of oligonucleotide primers for amplification of an allele which is associated with atopy, which allele is situated at a locus in a region of chromosome 13 of up to 1 megabase in length, which region contains the locus D13S273, but not including the region containing the locus D13S153.
11. The pair of oligonucleotide primers according to claim 10, one of which is labeled with a detectable marker.
12. The pair of oligonucleotides according to claim 10 or claim 11, capable of hybridising under suitably stringent conditions to a region either side of a region of microsatellite repeats at D13S273.
13. The pair of oligonucleotide primers according to claim 12, comprising the oligonucleotide sequences identified by SEQ ID NO: 1 and SEQ ID NO: 2 or similar sequences.
14. An assay kit which comprises the pair of oligonucleotide primers according to any one of claims 10 to 13.